Docket No.: RFU0001-100 (133123.101) Serial No.: 09/834,321 PATENT Filed: April 13, 2001

IN THE CLAIMS:

Please amend claims 1, 40, 42 and 43, and cancel claim 39.

This listing of claims will replace all prior version and listings of claims in the application.

1. (Currently amended) A method of enhancing cytotoxicity elicited by a therapeutic antibody in a subject, which method comprises disrupting activation of SHIP by Fc-gamma-receptor IIB (FcγRIIB) caused by binding of the antibody to FcγRIIB, wherein the disrupting is accomplished by modifying the Fc region of the antibody to reduce its affinity for FcγRIIB, thereby inhibiting binding of the antibody to FcγRIIB in the subject, wherein the Fc region of the antibody is at least 80% homologous with a native Fc region, and wherein said therapeutic antibody binds activating Fc-receptors with at least the same affinity as the wildtype antibody.

2-9. (Canceled)

10. (Original) The method according to claim 1, wherein the antibody is an anti-tumor antibody.

11. (Original) The method according to claim 10, wherein the antibody is specific for a tumor cell growth receptor.

- 12. (Original) The method according to claim 11, wherein the antibody is specific for a HER2/neu growth factor receptor.
- 13. (Original) The method according to claim 1, wherein the antibody is specific for a CD20 B cell antigen.

14. (Canceled)

15. (Previously presented) The method according to claim 1, wherein the subject expresses human Fc receptors.

16-22. (Canceled)

23. (Previously presented) The method according to claim 1, wherein the wherein the Fc region of the antibody is at least 90% homologous with a native Fc region.

24. (Previously presented) The method according to claim 1, wherein the wherein the Fc region of the antibody is at least 95% homologous with a native Fc region.

25. (Previously presented) The method according to claim 1, wherein the wherein the Fc region of the antibody comprises 1 amino acid substitution compared to the native Fc region.

26. (Previously presented) The method according to claim 1, wherein the wherein the Fc region of the antibody comprises 1-5 amino acid substitutions compared to the native Fc region.

27. (Previously presented) The method according to claim 25, wherein the wherein the Fc region of the antibody consists of 1 amino acid substitution compared to the native Fc region.

28. (Previously presented) The method according to claim 25, wherein the antibody is specific for a HER2/neu growth factor receptor.

29. (Previously presented) The method according to claim 25, wherein the antibody is specific for a CD20 B cell antigen.

30. (Previously presented) The method according to claim 1, wherein the wherein the Fc region of the antibody comprises 1 amino acid addition compared to the native Fc region.

- 31. (Previously presented) The method according to claim 1, wherein the wherein the Fc region of the antibody comprises 1-5 amino acid additions compared to the native Fc region.
- 32. (Previously presented) The method according to claim 30, wherein the wherein the Fc region of the antibody consists of 1 amino acid addition compared to the native Fc region.
- 33. (Previously presented) The method according to claim 30, wherein the antibody is specific for a HER2/neu growth factor receptor.
- 34. (Previously presented) The method according to claim 30, wherein the antibody is specific for a CD20 B cell antigen.
- 35. (Previously presented) The method according to claim 1, wherein the wherein the Fc region of the antibody comprises at least 1 amino acid deletion compared to the native Fc region.
- 36. (Previously presented) The method according to claim 35, wherein the wherein the Fc region of the antibody consists of 1 amino acid deletion compared to the native Fc region.
- 37. (Previously presented) The method according to claim 35, wherein the antibody is specific for a HER2/neu growth factor receptor.
- 38. (Previously presented) The method according to claim 35, wherein the antibody is specific for a CD20 B cell antigen.

Docket No.: RFU0001-100 (133123.101) Serial No.: 09/834,321 PATENT Filed: April 13, 2001

39. (Canceled)

- 40. (Currently amended) A The method of claim 1, enhancing cytotoxicity elicited by a therapeutic antibody in a subject, which method comprises disrupting activation of SHIP by Fcgamma-receptor IIB (FcγRIIB) caused by binding of the antibody to FcγRIIB, wherein the disrupting is accomplished by modifying the Fc region of the antibody to reduce its affinity for FcγRIIB, thereby inhibiting binding of the antibody to FcγRIIB in the subject, wherein the Fc region of the antibody is at least 80% homologous with a native Fc region, and wherein said therapeutic antibody retains binding to FcRIIA and FcRIIIA.
- 41. (Previously presented) The method of claim 40 wherein said retained binding is unchanged or enhanced as compared to the wildtype antibody.
- 42. (Currently amended) <u>A</u> The method of elaim 1, enhancing cytotoxicity elicited by a therapeutic antibody in a subject, which method comprises disrupting activation of SHIP by Fcgamma-receptor IIB (FcγRIIB) caused by binding of the antibody to FcγRIIB, wherein the disrupting is accomplished by modifying the Fc region of the antibody to reduce its affinity for FcγRIIB, thereby inhibiting binding of the antibody to FcγRIIB in the subject, wherein the Fc region of the antibody is at least 80% homologous with a native Fc region, and wherein said therapeutic antibody that has reduce reduced affinity for FcγRIIB has unchanged affinity for stimulatory FcRs, FcRI or FCRIII.
- 43. (Currently amended) <u>A</u> The method of elaim 1, enhancing cytotoxicity elicited by a therapeutic antibody in a subject, which method comprises disrupting activation of SHIP by Fcgamma-receptor IIB (FcγRIIB) caused by binding of the antibody to FcγRIIB, wherein the disrupting is accomplished by modifying the Fc region of the antibody to reduce its affinity for FcγRIIB, thereby inhibiting binding of the antibody to FcγRIIB in the subject, wherein the Fc

region of the antibody is at least 80% homologous with a native Fc region, and wherein said therapeutic antibody that has reduce reduced affinity for FcγRIIB has enhanced affinity for stimulatory FcRs, FcRI or FCRIII.

- 44. (Previously presented) The method according to claim 40, wherein the antibody is an antitumor antibody.
- 45. (Previously presented) The method according to claim 40, wherein the antibody is specific for a tumor cell growth receptor.
- 46. (Previously presented) The method according to claim 40, wherein the antibody is specific for a HER2/neu growth factor receptor.
- 47. (Previously presented) The method according to claim 40, wherein the antibody is specific for a CD20 B cell antigen.
- 48. (Previously presented) The method according to claim 40, wherein the subject expresses human Fc receptors.
- 49. (Previously presented) The method according to claim 40, wherein the wherein the Fc region of the antibody is at least 90% homologous with a native Fc region.
- 50. (Previously presented) The method according to claim 40, wherein the wherein the Fc region of the antibody is at least 95% homologous with a native Fc region.
- 51. (Previously presented) The method according to claim 40, wherein the wherein the Fc region of the antibody comprises 1 amino acid substitution compared to the native Fc region.

52. (Previously presented) The method according to claim 40, wherein the wherein the Fc region of the antibody comprises 1-5 amino acid substitutions compared to the native Fc region.

53. (Previously presented) The method according to claim 40, wherein the wherein the Fc region of the antibody consists of 1 amino acid substitution compared to the native Fc region.

54. (Previously presented) The method according to claim 40, wherein the wherein the Fc region of the antibody comprises 1 amino acid addition compared to the native Fc region.

55. (Previously presented) The method according to claim 40, wherein the wherein the Fc region of the antibody comprises 1-5 amino acid additions compared to the native Fc region.

56. (Previously presented) The method according to claim 40, wherein the wherein the Fc region of the antibody consists of 1 amino acid addition compared to the native Fc region.

57. (Previously presented) The method according to claim 40, wherein the wherein the Fc region of the antibody comprises at least 1 amino acid deletion compared to the native Fc region.

58. (Previously presented) The method according to claim 40, wherein the wherein the Fc region of the antibody consists of 1 amino acid deletion compared to the native Fc region.